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DEVELOPMENT AND DIFFERENTIATION OF THE TADPOLE EYE

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IN an earlier paper (Glücksmann 1930) it was shown that it is possible to explain the visible changes in form which take place during the development of organs of epithelial origin, in terms of certain cell processes. Thus, it was found that morphogenetic processes such as the invagination and folding of the epithelial tissues which form the optic cup and lens of the mammalian eye are the result of a co-ordinated series of cell movements, cell degenerations and orientated cell divisions. The question now arises as to how these different manifestations of cellular activity are, in fact, co-ordinated so as to ensure that an organ shall develop satisfactorily. Further, there is the problem of how the growth of such an organ is affected by the differentiation and mitosis of its cells and further of how such a regulation of cell processes can be brought about.

The answer to some of these questions was found by studying the early development of the eye of *Rana temporaria*. The tadpole eye is a particularly interesting subject for this type of investigation since the whole process of differentiation from the stage of the primary eye vesicle to that of the fully functioning organ is

accomplished so quickly. Whereas in the higher vertebrates the eye is not ready to function until near the end of the growth period, in the tadpole the differentiated parts have to function while the eye is still developing.

In the present paper the morphological changes which occur during the development of the tadpole eye will first of all be described. Later the problem of the regulation of the various cell processes which occur during morphogenesis and differentiation will be discussed.

Material and technique.—A lump of the fertilised frog spawn of *Rana temporaria* was taken from a neighbouring pond and kept in an aerated tank at room temperature. Batches of animals were killed at fixed time intervals over a period of ten days. In the period just after fertilisation a selection of eggs was taken every 5 hours but as the tadpoles got older the interval was increased to 17 and later to 24 hours.

Most of the material was fixed (direct from the tank) in either Zenker's or Susa fluid. A few specimens were fixed in formol and a few in Bouin's mixture. The embryos were embedded in paraffin and serial sections through the head were cut at 10 μ. The sections were stained by Feulgen's method (counterstained with a mixture of light-green and naphthol green) by Wilder's method or with haematoxylin and eosin. The material to be considered in the present paper consists of 224 tadpoles from the spawn of one individual and therefore presumably all fertilised at the same time, fixed at 13 different times during the ten days following removal from the pond. The number of embryos used for each fixation varied from 6 to 45. In addition some 80 tadpoles fixed directly from the pond in previous seasons were examined; the results do not differ in any way from those obtained with this year's material (1938).

Stages in the development of the tadpole eye.—In order to facilitate the presentation of the results the development of the eye, and more particularly of the retina, has been divided into 12 stages.

Stage 1. The stage of the primary optic vesicle. The cells contain both yolk and pigment, the latter accumulated on the internal surface of the vesicle. Two layers of dividing cells are found at this stage, one bordering the central surface of the eye vesicle while the other is situated between this and a layer of non-dividing cells at the other surface. (Plate 1, Fig. 1.)

Stage 2. The primary optic vesicle is elongated in a dorsal direction. The proximal wall of the vesicle which will later form the outer part of the optic cup appears stretched and thinner than the distal wall. There is no change in the distribution of mitotic cells or of pigment within the cells. (Fig. 2.)

Stage 3. The ectoderm covering the optic vesicle is thickened and begins to form the lens plate. The optic vesicle itself is further stretched and there is an increased thinning of the proximal wall. The distal wall has lost its spherical outline and has become flattened while its mitotic cells are now confined to one layer only, bordering the central surface of the vesicle. This layer will later become the outer layer of the developing retina (Fig. 3). Mitoses are present in the pigment epithelium throughout the period of development.

Stage 4. The lens appears as a shallow groove and the ectoderm composing it consists of three layers: (1) the unpigmented inner layer (the lens plate), (2) an intermediate layer of irregularly arranged pigmented cells, and (3) the pigmented outer or peridermal layer.

The transformation of the optic vesicle into the optic cup has begun, the proximal wall of the vesicle becoming the pigment epithelium and the distal wall the retina proper. The proximal wall has become further stretched so that the thickness of the pigment layer is only about one-fifth of that of the retina. The retinal cells still contain yolk and pigment but the latter now tends to accumulate at the inner surface of the retina. (Fig. 4.) The cells have become more conical in shape, the base of the cone in each case being on the outer surface and the apex pointing towards the inner surface of the retina.

Stage 5. The lens pit is deeper and the optic cup is further elongated towards the dorsal side, it has also become deeper changing its form from that of a plate to that of a bowl. The stretched pigment epithelium now adheres closely to the retina and is composed of only one layer of very flat cells. The amount of yolk in the individual cells steadily decreases during development and at this stage is greatly reduced as compared with stage 1. The pigment in the retinal cells is still accumulated at the inner surface of the retina (Fig. 5).

Stage 6. The lens is now connected to the epidermis by a stalk only. The eye has become more cup-like by a further dorsal elongation and a stretching of the pigment epithelium which is still in close contact with the retina. The retinal cells are irregularly arranged and many of the dividing cells appear pycnotic and degenerate. (Fig. 13.) These dying cells are confined to the central area of the retina and the mitotic cells in the periphery appear quite healthy. The retinal cells still contain yolk which can also be seen in the dividing cells both normal and pycnotic. Pigment is present in the retina but there is less in the central than in the peripheral parts, and it still tends to accumulate at the inner surface. (Fig. 6.)

Stage 7. In this stage the lens is separated from the epidermis.

In the central part of the retina the ganglion cells (recognisable by the larger size and fainter staining of their nuclei) can now be seen in a layer along the inner surface. Mitotic cells have completely disappeared from the outer region of the central part of the retina but are still to be seen in the periphery. These dividing cells are all quite healthy; in fact, practically no degenerate cells can be found in the specimens at this stage. The central part of the retina has also become denuded of pigment though there is still plenty at the inner surface in the periphery. The extreme periphery of the retina has begun to grow in towards the lens. (Fig. 7.)

Stage 8. The lens has now become a proper vesicle. The cells of the pigment epithelium are rather more cubical in shape than in the preceding stages and the layer as a whole has begun to be separated from the retina especially in the centre of the eye. A few fibres can just be seen separating the ganglion cells from the outer part of the retina. This is the first sign of the development of the inner fibre layer. Yolk remains in the retinal cells even in the differentiated ganglion cells but the amount of yolk present per cell is still decreasing. Very few degenerate cells occur but there is plenty of cell division in the periphery. The retinal pigment is confined to the extreme periphery at this stage. (Fig. 8.)

Stage 9. The development of the lens fibres has begun in the posterior wall of the lens vesicle. The pigment epithelial cells have become even more cubical than in stage 8 and the layer which contains a few degenerate cells is markedly detached from the retina. In the retina the inner fibre layer is now well marked and it is possible to distinguish inner nuclear cells outside it. In this region there are a great many degenerate cells which are restricted to the middle layers of the central retina, they are not found either in the ganglion cell layer or on the outer surface. (Fig. 14.) The extreme periphery is still characterised by the presence of pigment and of dividing cells neither of which occur anywhere else in the retina in this or the succeeding stages. (Fig. 9.)

Stage 10. The lens fibres have developed until they nearly fill the lumen of the lens vesicle. The central part of the pigment epithelium is still detached from the retina; the outline of the surface facing the retina has become irregular foreshadowing the development of the cell processes which later carry the pigment to and fro over the visual cells as the eye is light or dark adapted. In the centre of the retina the first few fibres of the outer fibre layer separating the inner nuclear from the outer nuclear layer can be seen. The outer nuclear layer is only one cell thick and the inner limbs of the visual elements have begun to differentiate

in a few places, although the cells are not yet regularly arranged. A few degenerate cells occur at the border of differentiation just on the inner side of the outer nuclear layer. In the inner nuclear layer a few spindle-shaped cells are present associated with fibres running through the retina towards its inner surface—these are the beginnings of Müller's fibres and supporting cells. At this stage the retina is clearly divided into a central differentiated and a peripheral undifferentiated area. The latter is further subdivided into the germinative zone containing dividing cells and a pigmented zone in the extreme periphery. The undifferentiated area is clearly marked by the occurrence of mitosis, the absence of visual cells and the smooth outline of the cells of the pigment epithelium. All the retinal cells are now practically free from yolk.

The pigmented part in the extreme periphery of the retina has turned further in towards the lens, preparatory to forming the iris. (Fig. 10.)

Stage 11. In the cornea the pigment has disappeared from the inner epidermal layer and is much decreased in the peridermal layer.

Fibres have now begun to form at the equator of the lens and the total number of lens fibres is much greater than before.

In the central area the cells of the pigment epithelium are drawn out into short pigmented processes pointing towards the retina.

In the retina itself the central area is by now almost fully differentiated. The nuclei of the visual cells (the outer nuclear layer) are arranged more regularly and the vacuoles of the visual elements are easily recognisable, while in the very centre short outer limbs are already visible. The outer fibre layer is well differentiated and the number of Müller's cells and fibres in the inner nuclear layer has increased. At the border of the differentiated and undifferentiated areas of the retina, degenerate cells may be seen in both the outer and inner nuclear layers where the two layers meet in the germinative zone.

The iris is much more pronounced at this stage. (Fig. 11.)

Stage 12. The differentiation of the tadpole eye is completed at this stage, and until metamorphosis the only further change is enlargement caused by cellular multiplication.

Pigment disappears completely from the cornea and in the retina the outer limbs of the visual cells are at last fully differentiated. These outer limbs are separated from one another by the cell processes of the pigment epithelium. The division of the retina into a central differentiated zone, an intermediate germinative zone and the peripheral pigmented zone of the iris still persists. Since mitosis is confined to the germinative zone

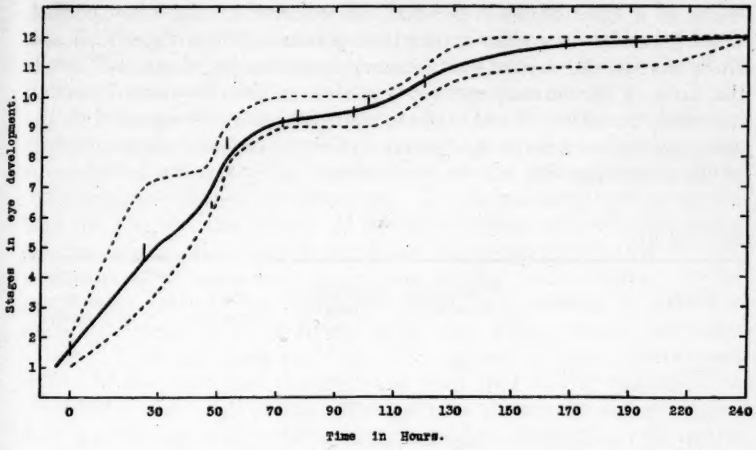
and since the number of cells in the central area and particularly in the inner nuclear layer continues to increase it is obvious that cells must migrate into this region from the germinative zone. Until metamorphosis there is a progressive change in the general shape of the eyeball. This can be seen in diagram 1 in which camera lucida drawings of the outlines of the eye at various stages have been superimposed on one another. An idea of the increase in size of the different layers of the retina is also given by the diagram.

TABLE I

Time	Stages												Total	Stage	Average
	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII			
0 hrs.	4	7	—	—	—	—	—	—	—	—	—	—	11	1·63	±·13
25 ,,	—	—	4	17	7	13	4	—	—	—	—	—	45	4·9	±·17
48 ,,	—	—	—	—	—	27	6	4	—	—	—	—	37	6·37	±·10
53 ,,	—	—	—	—	—	—	—	6	5	—	—	—	11	8·45	±·13
72 ,,	—	—	—	—	—	1	—	—	19	8	—	—	28	9·17	±·13
77 ,,	—	—	—	—	—	—	—	—	10	6	—	—	16	9·37	±·10
96 ,,	—	—	—	—	—	—	—	1	12	16	—	—	29	9·51	±·10
101 ,,	—	—	—	—	—	—	—	—	2	10	—	—	12	9·83	±·08
120 ,,	—	—	—	—	—	—	—	—	—	4	5	—	9	10·5	±·15
144 ,,	—	—	—	—	—	—	—	—	—	—	—	5	5	12·0	—
168 ,,	—	—	—	—	—	—	—	—	—	—	1	5	6	11·83	±·13
192 ,,	—	—	—	—	—	—	—	—	—	—	1	6	7	11·86	±·10
240 ,,	—	—	—	—	—	—	—	—	—	—	—	8	8	12·0	—

In calculating the standard deviation of the mean stage at each age (last column) Shepherd's correction for grouping was applied, since only integers were used in assigning stage numbers to the individual animals.

The time relations of the stages of development.—Table I shows the number of specimens in each stage of development which was found at each fixation time. From these figures the stage average reached at any given time interval after the first fixation of material has been calculated and an average figure for the duration of each stage obtained. These figures are plotted in Graph I where the solid line represents the average stage achieved at any given time and the two dotted lines the most advanced and the most backward stage observed. It is evident that, in general, the variation in the stage of development reached at any given time is relatively small. There is one interval, however, for which this generalisation does not hold. At 25 hours there is a considerable variation in the development since all stages from 3 to 7 were found at this time. Of the tadpoles fixed at this interval some were hatched and some were not, and it was found that the hatched material tended to be more advanced than the



GRAPH 1.

Showing the average stage (continuous line) in eye development reached at any given time interval after the first fixation of material. The two dotted lines represent the most advanced and the most backward stage observed.

unhatched. Thus, 25 hours after the first fixation of material the stage average for unhatched animals is 3·7 ± 0·15 while that for the hatched animals is 5·2 ± 0·16. After this period the variation in the stage found at any given time is again reduced so that one must assume that the process of hatching has some effect on the rate of development, in other words, those tadpoles which are late in hatching are also late in development and have to make up leeway after they are hatched.

From Graph I the average time taken before each stage is reached can be read and from this one can calculate the average duration of each stage. It will be seen that there is a distinct flattening of the curve between stages 5 and 7 and between stages 8 and 10, in other words stages 6 and 9 are reached later than one would expect from the general shape of the curve. It seems significant that this retardation in the rate of development should occur at the stages in which an unusual number of degenerate cells are present.

Cell size and the area of the retina.—The volume of the eye can be calculated by area measurements taken from photographs at a constant magnification of x 175 of eyes at different stages. Such area measurements for stages 1, 2, 3, 8 and 9 are given in Table II. During the period of invagination there is little increase in the

total volume of the tadpole eye. In mammals, on the other hand, there is a considerable increase in volume during this period. Data given in an earlier paper (Glücksmann 1930, Figs. 2, 5, 24) show that in the mouse eye the area increases by about x2·3 while the area of the human eye (over a shorter developmental period) increases by x1·5. If the layer of marginal fibres is ignored in the area measurements for the human eye the increase in area amounts to x2 in comparable stages.

TABLE II

TADPOLES

Stage	Area	Total Cell Number	Average Area	Average Cell Number	Proportion Area to Cell Number
I	556	67			
II	994	82	775	74·5	10·4
III	600	103			5·8
VIII	730	225			
IX	784	307	757	226	2·9

Area measurements in square millimetres at a magnification of ×175.

MICE

Figure	Area in square millimetres at a magnification of ×350
2	397
5	473
24	914

Figure 2 is comparable to Tadpole Stage II
„ 24 „ „ „ IX

In both the mammalian eyes investigated (mouse and human) there was no appreciable change in the size of individual cells and the increase in the volume of the eyeball was due to an increase in the number of cells contained in it. In the tadpole the number of cells also increases during development but in spite of the fact that there are 3·5 times more cells present in the retina at stages 8-9 than there are in stages 1-2, the volume of the eye remains practically unaltered. This is possible because the increase in cell number is associated with a decrease in cell size so that at the later stages the size of a cell is only about $\frac{1}{3}$ of that

of a cell at the earlier stage. The decrease is largely due to the reduction of the yolk content of the individual cells. In other words, the slowly decreasing amount of yolk available is distributed among a greater number of cells and each cell therefore contains less yolk and is smaller in consequence.

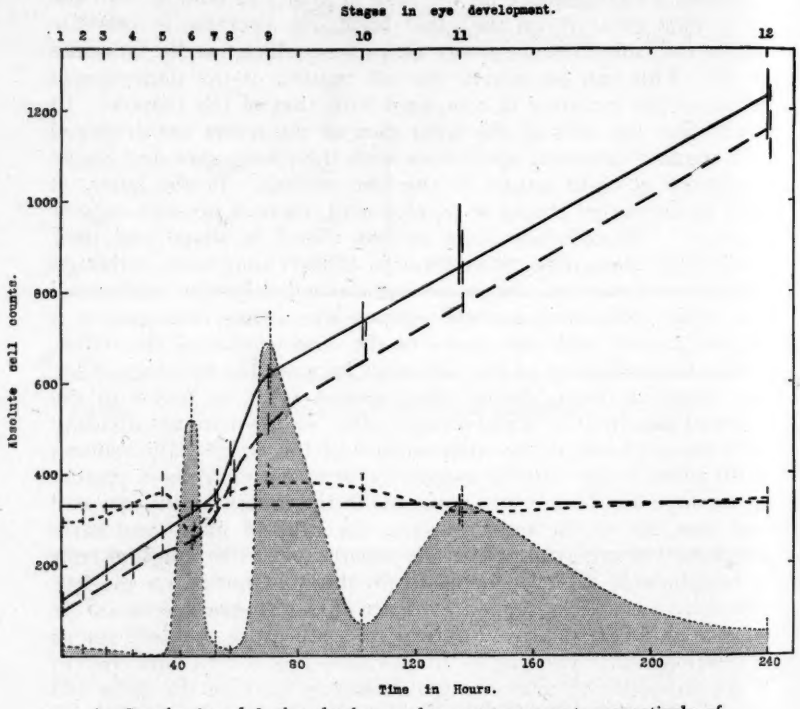
The invagination of the optic cup.—The decrease in cell size due to the diminution of yolk content in amphibian embryos has a profound effect on the mechanism of the invagination of the optic vesicle to form the optic cup. In the mammal this invagination is largely the result of a combination of morphogenetic degenerations which leave room for cell movements and the cell divisions which produce an increase in area and volume. In the amphibian embryo, on the other hand, the decrease in cell size allows the cells to move freely in an area which hardly increases at all. This can be seen if the cell pattern of the undeveloped retina of the mammal is compared with that of the tadpole. In the former the cells of the outer part of the retina are arranged as a regular columnar epithelium with their long axes and nuclei orientated at right angles to the free surface. In the latter, at least in the earlier stages of development, there is no such regular pattern. The cells are more or less round in shape and their nuclei only show a slight orientation of their long axes, although later as invagination progresses and the cells decrease in size and lose their yolk, they become shaped like cones arranged in a regular pattern with their bases on the outer surface of the retina.

Another indication of the difference between the structure of the two types of retina during development is to be found in the different distribution of the mitotic cells. In the mammal dividing cells are confined to the outer surface of the retina (Glücksmann 1930) while in the tadpole another layer of mitotic cells is present up to stage 3. This layer is situated in the middle of the eye wall and here, as on the outer surface, the cells in meta- and early anaphase are spherical. Also the separation of the daughter cells in telophase is achieved as easily in this position as on the free outer surface which is good evidence that cell movements in the tadpole retina are relatively unrestricted, at least in the early stages of development. Here again the decrease in size and yolk content is accompanied by a more regular arrangement of the cells and by the restriction of mitosis to the free surface of the retina.

It is evident, therefore, that because of the initial yolk content and subsequent decrease in cell size, the space for the cell movements required for changes in the form of the eye is available in the tadpole without the necessity for morphogenetic degenerations. There is another factor which restricts free movements at least in the human retina, which is absent from the tadpole. In the human embryo there is a network of fibres in an area free from cell nuclei

at the inner surface of the retina—the so-called marginal layer. This net-work of fibres which must obviously emphasise the rigid arrangement of the cells and restrict their movements is not present in the tadpole eye during its invagination.

The actual process of invagination is also modified in the amphibian as compared to the mammalian eye. This is especially noticeable in the rapid disappearance of the primary lumen of the optic vesicle and in the configuration of the pigment epithelium in the tadpole. The optic vesicle stretches considerably in the dorsal direction before invagination thus narrowing the lumen,



In Graphs 2 and 3, the absolute and percentage counts respectively of mitotic and degenerate cells are plotted at a scale ten times that of the natal and resting cell counts respectively.

GRAPH 2.

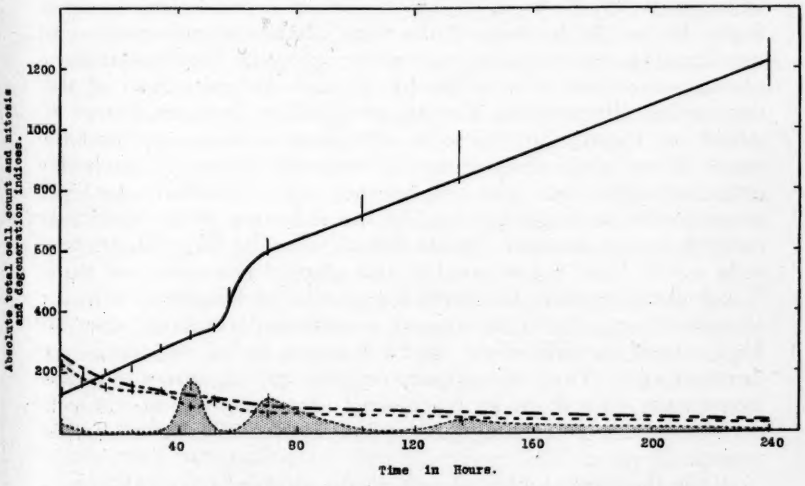
Showing the absolute counts of total, resting, dividing and degenerate cells with their standard deviations in different stages of eye development.

———— total number of cells. ——— ——— resting cells.
— — — — dividing cells, ——— — ——— calculated number of dividing cells. Stippled area — degenerate cells.

while at the same time the pigment epithelium is thinned until it becomes a single layer of flat cells. The transformation into the optic cup is then achieved not so much by an actual bending of the retinal wall as by the elongation of its peripheral parts. In the human embryo, on the other hand, the lumen of the primary optic vesicle is only slowly reduced by the inward folding of the retina while the pigment layer retains its thickness. This process in the human is bound up with a considerable increase in the total size of the eye whereas in the tadpole there is no appreciable change in volume at this stage.

Quantitative Analysis of the Cell Processes Involved in the Early Development of the Tadpole Eye

For this purpose some typical specimens at each stage of development was selected and the number of resting, dividing and degenerating cells was counted in two central sections through each eye. The sections chosen were those through the papilla and the choroid fissure. The means and standard deviations of the counts for each stage were determined and the results plotted (Graphs 2 and 3). Graph 2 shows the absolute counts of total,



GRAPH 3.

Showing the absolute total cell count, the degenerative index and the calculated and observed mitotic indices.

———— total cell count. — — — — observed mitotic index. —— — —— calculated mitotic index. Stippled area — degenerative index.

dividing and degenerate cells with their standard deviations while the mitotic and degenerative indices for each stage are plotted in Graph 3. The mitotic index is given by the number of mitotic cells divided by the total number of cells while the degenerative index is, similarly, the number of degenerate cells divided by the total cell count. As can be seen from the graphs there is a steady increase in the total number of cells and also in the number of resting cells present from stage 1 to stage 6 and again from stage 9 onwards. This increase amounts to about 50 cells in 10 hours for the first period and to about 40 cells in 10 hours for the later period. Between stages 6 and 7 the increase in the total cell count is slowed down and this is followed by a considerable acceleration from stage 7 to 8, which, again, falls off slightly between stages 8 and 9.

The number of mitotic cells remains fairly constant throughout the development of the retina except in stages 5, 6, 8 and 9 where significant variations are observed. The mitotic cell count is low in stage 6 and high in stages 5, 8 and 9. The reduction in the rate of increase of the total cell count in stage 6 seems to be due to the small number of mitotic cells present at this stage but it is not always possible to correlate a high rate of total cell increase with a high mitotic count. For instance, the mitotic counts found in stages 8 and 9 are no higher than those found between stages 9 and 10 but the increase in the total number of cells present is considerably greater during the earlier period. The explanation of this discrepancy is to be found in a consideration of the degenerate cells present. The degenerate cells observed in stage 9, which are included in the total cell count, have disappeared by stage 10 and their absence accounts for the failure to reach the expected higher total cell count for this stage. Similarly the high mitotic index at stage 5 decreases the reduction in the total cell count for stage 6 which should follow from the large number of cells which have degenerated at this stage. On the other hand it is doubtful whether the slight increase in the number of mitoses observed from stage 6 to stage 7 is sufficient to account for the high rate of increase in the total cell count during this period of development. This discrepancy might be explained by the assumption that there is a speeding up of the process of cell division and a shortening of the interkinetic interval over this period.

While the total number of cells increases steadily and the number of mitotic cells remains fairly constant during development, the degenerate cell count rises in three distinct peaks. Only the first of these waves of degeneration, that which occurs at stage 6, is associated with a marked decrease in the mitotic cell count. The second peak (stage 9) coincides with a period of relatively

high mitotic activity and the third is not associated with any change in the number of mitotic cells.

Some additional information is given by Graph 3. It shows, for instance, that the first wave of degeneration in stage 6 is the highest in proportion to the total cell count. Further it indicates that at stage 6 there is a significant difference between the mitotic index calculated for a steady increase in total cell count and that which is actually obtained. For the rest of the developmental period there is a fairly good correspondence between these two curves. The calculation of the mitotic index is based on the assumption that of the two daughter cells resulting from one cell division one divides again while the other becomes a resting or differentiating cell. The fact that the actual number of mitotic cells remains so constant throughout seems to justify this assumption. The statistical analysis of results given in Graph 3, with the exception of those for stage 6, also points to this being the true interpretation.

As described above, mitotic cells are fairly evenly distributed over both the central and peripheral regions of the retina during development from stage 1 to stage 6. In stage 6 the dividing cells of the central retina become pycnotic and degenerate and from stage 7 onwards this area remains free from mitoses. In spite of the fact that a large percentage of the dividing cells degenerates in stage 6, the mitotic cell count for the whole retina is able eventually to return to normal and therefore it is obvious that both the daughter cells of those divisions which are successful at this stage must divide again. In addition the interkinetic interval may be shortened, that is cells might begin to divide sooner after their last mitosis and therefore during a period when they would normally be resting. In this way cells from the peripheral retina are made available to replace those which have been lost from the centre. Thus there is a complete reorganisation of the dividing cells in stage 6.

Cell degeneration.—The first wave of degeneration begins at the outer surface of the retina among the dividing cells and is first detectable by a pycnosis of the chromatin material which usually appears during meta- or anaphase. As the degeneration proceeds to chromatolysis these cells move towards the inner retinal surface where they finally disappear, either as a result of intracellular absorption by neighbouring cells or by complete dissolution. The details of the degenerative process need not be described here as they have already been dealt with in earlier papers (Glücksmann 1930; Spear and Glücksmann 1938). During the later phases of stage 6 some ganglion cells, conspicuous on account of their larger size and the fainter staining of their nuclei, can be recognised for the first time among the degenerate

cells on the inner surface of the retina. This process of degeneration and migration of degenerating cells is confined to the central area of the retina.

The second wave of degeneration affects the cells of the middle zone of the central retina in the position which will later be occupied by the inner nuclear layer. The degenerative process starts during the resting phase of these cells—there are no mitotic cells in this layer—and passes through the usual stages of chromatopycnosis, hyperchromatosis and chromatolysis (see Spear and Glücksmann, 1938). Sometimes this process is associated with pigment formation and this is very conspicuous since the pigment found in the retina during early development has already disappeared from the central area. There seems to be a considerable individual variation in the number of cells which degenerate at this stage. In some eyes there are so many that they cause a rupture of the outer surface of the retina towards the pigment epithelium and cells are extruded into the lumen of the optic vesicle. With the resorption of these cells, which occurs during the later phases of stage 9, the retina recovers its orderly pattern and only a few pigmented patches remain to bear witness to the disorganisation that was caused by the presence of excessive numbers of degenerate cells. The rupture of the retina which often follows the accumulation of large numbers of degenerate cells is a result of the tendency of these cells to congregate in the same place (Glücksmann, 1930; Glücksmann and Tansley, 1936). Finally the pigmented remnants also disappear although traces of them can sometimes be found in stage 10 and even as late as stage 11.

Simultaneously with the appearance of the second degeneration wave in the retina, degenerate cells can be found in the pigment epithelium and here again they are restricted to the central area. The dead cells of both the first and second degeneration waves contain roughly the same amount of yolk as is present in the normal cells at these stages of development.

The central parts of the retina are not involved in the third wave of degeneration which occurs in stage 11. The cells concerned are restricted to the border between the central, differentiated retina and the germinative zone and in this area they are found in the outer nuclear layer and the outer part of the inner nuclear layer. The degeneration of these cells also begins in the resting phase but does not result in pigment formation. Mitotic cells are rarely involved.

Cell Division.—It has already been pointed out that the number of mitotic cells remains almost constant throughout the period of development under consideration and that, except during stage 6,

it is very probable that only one daughter cell divides again. During the first stages of development there are two layers of dividing cells in the retina but later on these are restricted to the outer surface. In the earlier period pigment and yolk are regularly found in the dividing cells to much the same extent as in the resting cells.

Since only one of the daughter cells of a mitosis divides again the other has to migrate into the differentiated parts of the retina which in the later stages of development usually means into the inner nuclear layer. That the other daughter cell also leaves the outer surface is shown by the fact that this area contains only mitotic cells. The second daughter cell must, however, return to the outer surface for its own division later.

It is known that the mitotic cells of the developing retina tend to show a definite orientation of their axes (Glücksmann, 1930). In the tadpole the distribution of position in stage 12 was found to be as follows: 82·2 per cent. lay with the axis of mitosis parallel to the outer surface of the retina, and 17·8 per cent. with their axes at right angles to the outer surface. There is, therefore, a marked preference for a plane parallel to the outer surface of the retina in which both daughter cells lie at the free surface of the epithelium. In only 17·8 per cent. of all cell divisions does one daughter cell lie at the free surface and the other nearer the inner surface of the retina.

Cell movement.—The shape of a cell and its movements are closely associated. Thus, changes in its external form are caused by movements of its protoplasm and at the same time movements of the cell as a whole are brought about by suitable changes in its shape; in other words the cell is capable of movement by changes in its form. The reality of movements within the cell is shown by the changes in the distribution of pigment during the early stages of the development of these retinae. In the very young eye the retinal cells are ellipsoid in shape and the pigment is concentrated on the outer surface of the retina but when, during development, the cells become conical and their apices point inwards the pigment changes its position and collects on the inner surface of the retina. Whenever there is any change in the external form of a cell the pigment within it tends to accumulate at the narrowest part.

The appearances by which the movement of a cell may be recognised by the shape and staining power of its nucleus have already been described (Glücksmann, 1930) and it is not necessary to consider the subject in detail again here. Briefly it was found that if there is no obstruction by external factors, the nucleus becomes stream-lined in the direction of movement and the

anterior pole can be recognised by the faintness with which it stains.

In addition to the movements of resting cells there are migrations of dividing cells, both before and after mitosis, and also of degenerate cells. The movements of mitotic cells have already been dealt with to some extent earlier in this paper but those of the degenerate cells must now be described.

Degenerate cells always show a tendency to congregate; in stage 6 for instance, they become concentrated on the inner surface of the retina while in stage 9 they mostly occur near the outer surface. In stage 6 all the cells in the early stages of degeneration are situated at the outer surface (they originate as dividing cells) and only those in the terminal stages of degeneration are to be seen at the inner surface. It is clear, therefore, that these cells must move inwards through the retina while they are in the process of degenerating. In some cases the movement is really accomplished by normal resting cells which pick up the degenerating remnants and carry them to the inner surface but there are also free remnants present which must somehow have made the journey by themselves. These degenerate cells are round and liquified and seem to float rather than to move actively. They may either be dissolved intercellularly or be resorbed by neighbouring cells when they reach the inner surface.

In stage 9 the degenerating cells show a tendency to congregate on the outer border of the inner nuclear layer and as stated above this may lead to bulging and even to rupture of the outer surface of the retina. Thus, the degenerating cells of stage 9 move in the opposite direction to those of stage 6.

During early development in the tadpole there is a rapid change in the form of the eye and the arrangement of the retinal cells is very irregular. Before stage 7, when a regular epithelial pattern of cells first appears in the centre, the cells of the retina, although showing signs of orientation in the radial direction, tend to lie at all angles to each other and exhibit the characteristic signs of movement. The direction of these movements differs in different parts of the retina and depends on the changes in form of the eye. Thus, in the central retina at stage 6 and also early in stage 7 there is a noticeable movement of cells towards the inner surface.

It is not until stage 12 is reached that the cell movements really become regulated in relation to the whole retina. At this stage the retina is divided into the iris, the germinative zone to which the dividing cells are confined and the central differentiated area. Under these conditions the differentiated parts of the retina are dependent on the germinative zone for their supply of new cells. Since the number of cells in the central retina continues to increase and since this area contains no mitoses there must be a movement

of cells into the area from the germinative zone. There is also morphological evidence for such migrations into the central retina. On the border between the germinative and differentiated zones cells may be found in the outer part of the inner nuclear layer lying at right angles to the main radial axis, and such cells can be traced right into the central parts of the retina where they are present throughout the inner nuclear layer. Some of these cells then migrate through the outer fibre layer to become visual cells. All the stages of this journey from the germinative zone to the outer surface of the central retina are easily recognisable and the appearance of the cells as they make their way through the outer fibre layer is very similar to that observed in an earlier investigation on the olfactory epithelium (Glücksmann, 1930). These migrating cells of the retina are affected in the fasting experiments already reported by Spear and Glücksmann (1939).

It should be relatively easy for the cells situated at the outer part of the edge of the differentiated region to migrate directly into the outer nuclear layer and for those at the inner surface to move into the ganglion cell layer. Both these migrations do, in fact, occur and the moving cells are easily recognised by their shape and also by the staining of their nuclei. Towards the periphery the cells of all three nuclear layers are much more irregular in their arrangement and the layers themselves are thicker than in the centre; this difference is especially marked in the earlier periods of development before metamorphosis. In the amphibian eye the inner nuclear layer always remains thicker than the outer nuclear layer because it harbours not only its own ganglion and supporting cells but also acts as a store house for future visual cells.

Diagram 1 shows that the change in general form of the eye also involves the differentiated central retina and especially the outer nuclear layer which elongates considerably during development. This increase in length of the outer nuclear layer is due to an increase in the number of its cells and it has already been shown that this is achieved partly by the simple addition of cells at the peripheral border from the germinative zone and partly by the acquisition of cells which also originate in the germinative zone but reach their destination in the centre via the inner nuclear layer and then across the outer fibre layer. The ganglion cell layer also increases in length but there is no evidence that this increase is due to additions to its cell population from the inner nuclear layer. It is, in fact, impossible that this layer should acquire many new cells during development since its increase in length is accompanied by an increase in the distance between individual ganglion cells. There is, however, some addition of cells to the periphery direct from the germinative zone.

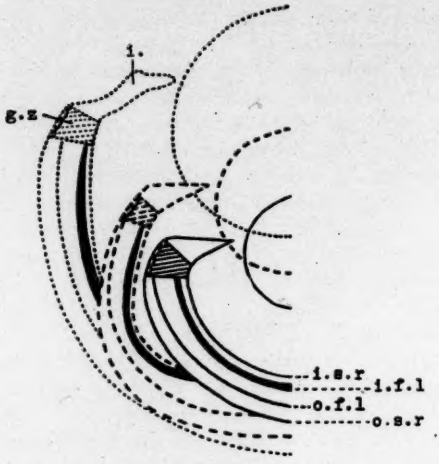


DIAGRAM 1.

Camera lucida drawings of the outlines of the eye have been superimposed to show the progressive change in the general shape of the eye.

During development the inner nuclear layer not only provides a path along its outer part for cells moving from the peripheral to the central retina but also acts as a storehouse for undifferentiated cells.

Discussion

The possible part played in the morphogenesis of organs by such cell activities as mitosis, movement and degeneration, has attracted little attention. In 1914 Gurwitsch showed that cell division and cell movement may be responsible for changes in the form of an organ and both he and his pupils have since provided further evidence to support this idea. On the other hand Glaser (1914) in a much quoted paper arrived at the conclusion that morphological changes are not dependent on such cell processes but rather on differences in the absorption of water. He based his conclusions on an analysis of the folding of the neural tube in *Cryptobranchus alleghiensis* and also on observations of the changes of acidity which occur during the early development of the eggs and embryos of *Rana pipiens* and *Amblystoma punctatum*. The case of *Cryptobranchus* is exceptional since in this species there is an increase both in total volume and cell size without any increase in the number of cells present and it is

possible therefore that water absorption does in fact play some part in this instance. The changes in acidity which occur in *Rana pipiens* and *Amblystoma punctatum* were thought by Glaser to explain the mechanism of water absorption by causing surface effects but in this case he ignored the significance of the decrease in cell size which takes place during the development of these species. It should be noted that Glaser apparently overlooked the importance of considering mitosis and cell degeneration in any investigation of the development of tissues. He did not in fact examine any histological preparations of his material from *Rana pipiens* and *Amblystoma*, nor does he record whether cell divisions or degenerations were present in the sections of *Cryptobranchus* which he investigated.

In 1930 the present author showed that in mammalian organs which increase in volume and cell number while the cell size remains constant, there is a very definite relationship between changes of form and the cell processes of mitosis, degeneration and movement, and it was established that such cell activities always precede the change in form. The present investigation is concerned with an organ which does not change in volume during development but in which the cell number increases while the cell size decreases. Although, in the present case, a correlation can be found between cell movements and division and morphological changes in the eye, the absence of true morphogenetic degeneration is very evident. This difference between the mechanism of morphogenesis in mammals and in amphibia is undoubtedly due to the presence of yolk in the amphibian cells. It has already been pointed out that the presence of yolk and its progressive dilution by distribution among an increasing number of cells makes a freer epithelial arrangement possible in the amphibian retina. In this eye, also, the cells can move in a relatively unrestricted way whereas in the mammalian eye with its more rigid epithelial pattern such movements become possible only if some of the cells degenerate. Thus, the yolk content of developing amphibian cells is not only responsible for the different forms of gastrulation characteristic of these animals (Rabl, 1897) and for the different degree of differentiation of the muscular system (Glücksmann, 1934) but also for the different mechanism of such morphogenetic processes as folding, bending and invagination.

It has been clearly demonstrated above (and in the case of mammals in an earlier paper (Glücksmann, 1930)) that mitotic cells do not lie about haphazard but that they are very definitely orientated. This orientation both of the position of dividing cells and of cell movements must be under some sort of directing influence if the orderly development of the organ is to be safeguarded, and we have now to discover, if possible, how all these

processes are regulated and correlated one with another. The suggestion that cells may act independently of one another according to a preconceived harmony, probably transmitted by their genes—a possible explanation of self-differentiation can be dismissed as highly improbable. On the other hand, if the cells of an organ depend on each other and are all directed from outside, the question arises as to what influences are responsible, how they act and where they originate. That one organ may, in fact, be dependent on such influences from another is well known from the recent work on induction and organisers.

Lewis (1907/8) has shown that transplantation of the amphibian eye into other parts of the body does not prevent its normal development even when the removal is effected before the eye has reached the first stage described in this paper. Thus, even at this very early stage the amphibian eye appears to be capable of self differentiation, so that one must look for the factors which determine its development in the eye itself. This does not mean, however, that all the parts of the eye are already determined at this stage since most of these exhibit great powers of regeneration (Stone and others, 1937).

In our inquiry into the nature of these influences the three waves of degeneration which appear during the development of the retina provide a useful clue. Each of these waves precedes the differentiation of a new retinal layer and corresponds in its localisation to that differentiation. Thus, the first wave is followed by the appearance of the ganglion cells, the second by that of the inner nuclear cells and the third by that of the visual cells. The first degenerations affect mitotic cells only and after this wave has passed no more cell divisions are to be found in the area concerned. It seems probable that the factor or factors responsible for the differentiation of this part of the retina also exert an inhibitory effect on cell division and, further, that those cells which have already begun to divide when these influences are first exerted are destroyed. It is possible to explain the other two degeneration waves in a similar manner, only in these it is differentiating instead of dividing cells that are affected. For instance, the cells which degenerate during the second wave are those which are in the process of becoming ganglion cells and are unable to survive the influence which determines the differentiation of inner nuclear cells. In the same way the third wave of degeneration occurs because those cells which have now begun to develop into inner nuclear cells are overtaken by the new impulse to differentiate into visual cells, and die. The coincidence of each wave of degeneration with the beginning of a new type of differentiation seems significant enough to justify the

hypothesis just outlined. Also, as soon as one process of differentiation is thoroughly established there is no more degeneration until the next type of differentiation begins and this again indicates that the cells degenerate because they are unable to withstand the conflict between two different impulses to differentiate. When, later, one or other of the impulses predominates the cells are no longer faced with this unendurable conflict and are able to differentiate in the required manner.

We now have to inquire into the origin of these differentiation impulses. It is obvious that they are present within the eye and must, therefore, be intrinsic in the retinal cells. It is known that failure to differentiate in the normal fashion can be genetically controlled and it seems reasonable, therefore, to assume that genetic factors may be responsible for differentiation and that these factors may come into play only at suitable periods of development. (Goldschmidt, 1938.) If this assumption is correct the gene or gene complex which is normally bound to the chromatic material of the nucleus must also be able to exert its influence on neighbouring cells thus producing a field of differentiation.

Since size as well as differentiation is known to be genetically controlled the same mental picture can be used to explain the early stages of development when only multiplication of cells occurs. Here the regulating process seems to be relatively simple and to result in only one of the daughter cells of a mitosis being able to divide again. The differentiation of the central retina in stage 6 upsets this arrangement but it is soon re-established in the periphery in stage 7. To explain the orientation of cell movements and of the axes of the mitotic cells one may perhaps assume that this is due to the influence of the ultra-structure as postulated by Weiss (1933). Since it has been shown, however, that even morphological form is genetically controlled it may be that such a control is also responsible for the orientation of the ultra-structure.

Summary

1. The development of the tadpole eye and especially of the retina is described from the stage of the primary optic vesicle to that of the fully differentiated organ. For convenience the developmental history is arbitrarily divided into twelve morphological stages. The duration of each of these stages is calculated.

2. Counts have been made of the number of resting, dividing and degenerating cells in the retina at each stage of development,

and the inter-relation and significance of such cell activities is discussed.

3. The decrease in yolk content and consequent decrease in cell size during retinal development is described and the effect on the process of development of the amphibian eye is compared with its development in the mammal where the cells do not contain yolk.

4. Except in one stage of development the number of mitotic cells in the tadpole retina remains remarkably constant while the total cell count steadily increases. This suggests that only one of the daughter cells resulting from a mitosis can divide again. During the earlier development, dividing cells are distributed along the free outer surface of the whole retina but later they are restricted to the outer surface of the germinative zone. This change is marked by a transient fall in the total number of mitoses caused by the degeneration of the dividing cells of the central retina.

5. Three distinct waves of cell degeneration are observed during the development of the retina. The first is due to the death of the dividing cells of the central retina and is followed by the appearance of ganglion cells in this area. The second wave involves the resting cells of the future inner nuclear layer and precedes the differentiation of this layer, and the third is caused by the death of resting cells of the outer nuclear layer and occurs immediately before its appearance. The cells concerned in these waves of degeneration seem, therefore, to be those which are caught by the new differentiation impulse after they have already begun to obey the last.

6. Owing to the progressive decrease in cell size consequent on the decreasing yolk content, cell movements are unrestricted during the early development in the tadpole. After the division of the retina into a central differentiated area and a peripheral germinative zone, cell movements are mostly confined to migration from the germinative zone into the inner nuclear layer and from this into the outer nuclear layer.

7. The importance of these cell activities in determining the course of the morphogenetic changes which occur during the development of the amphibian retina is discussed and an attempt is made to determine the origin of the factors which are responsible for the co-ordination of all cell activities into an orderly pattern which will ensure the proper development of the eye as a whole.

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LIST OF ABBREVIATIONS.

d	dorsal	m	mitosis
dc	degenerate cells	ogc	opticus ganglion cells
gz	germinative zone	ofl	outer fibre layer
i	iris	onl	outer nuclear layer
ifl	inner fibre layer	osr	outer surface of the retina
inl	inner nuclear layer	p	pigment epithelium
isr	inner surface of the retina	pw	proximal wall of the optic vesicle
lp	lens plate	ve	visual elements

DESCRIPTION OF PLATES

All the figures are photomicrographs. Figures 13 and 14 are taken from areas outlined in Figures 6 and 9 respectively. A magnification of x 175 was used for Figures 1–12 and of x 775 for Figures 13 and 14.

Cross sections of the tadpole are cut at 10μ thickness, stained by Feulgen's method and counterstained with a mixture of light green and naphtholgreen.

FIG. 1. Stage of the primary optic vesicle. Note the two layers of mitotic cells (m) and the accumulation of pigment on the internal surface of the vesicle.

FIG. 2. The primary optic vesicle is elongated in a dorsal direction (d). The proximal wall (pw) of the vesicle is thinner than the distal wall.

FIG 3. The optic vesicle is further stretched and the thinning of the proximal wall (pw) increased. The lens plate (lp) is visible as a thickening of the ectoderm.

FIG. 4. The transformation of the optic vesicle into the optic cup has begun. In the retina the pigment tends to accumulate on the inner surface (isr). The lens plate (lp) is transformed into a shallow groove.

FIG. 5. The transformation of the optic vesicle into the optic cup is completed. The pigment epithelium (p) adheres closely to the retina. The decrease in yolk content of the retina is indicated by the closer packing of the nuclei. The lens pit is deepened.

FIG. 6. The lens is connected to the epidermis by a stalk only. The eye has become more cup-like by a further dorsal (d) elongation. Pigment in the retina is accumulated at the inner surface (isr). *Cf.* Fig. 13.

FIG. 7. In the central part of the retina ganglion cells (ogc) are seen in a layer along the inner surface (isr). In this central zone pigment and dividing cells have disappeared. Mitosis and pigment, however, is present in the peripheral parts of the retina. The pigment epithelium (p) consists of a thin layer of flat cells.

FIG. 8. The lens has now become a proper vesicle. The cells of the pigment epithelium (p) are more cubical in shape. This layer as a whole is detached from the central parts of the retina. The differentiation of the opticus ganglion cell layer (ogc) has progressed.

FIG. 9. The development of lens fibres has begun. In the central parts of the retina the inner fibre layer (ifl) is visible. *Cf.* Fig. 14.

FIG. 10. The pigment content in the central part of the cornea is decreased. The central part of the retina is differentiated into the opticus ganglion cell layer (ogc), the inner nuclear layer (inl) and the outer nuclear layer (onl). The outer fibre layer (ofl) is now marked. The inner limbs of the visual elements (ve) have begun to differentiate. The outline of the inner surface of the pigment epithelium (p) has become irregular foreshadowing the development of cell processes.

FIG. 11. In the cornea the pigment has disappeared from the inner epidermal layer and much decreased in the peridermal layer. In the centre of the retina the visual cells are more regularly arranged; the vacuoles and short outer limbs of the visual elements (ve) are now visible. At the border of the differentiated and undifferentiated areas of the retina degenerate cells (dc) are found. The peripheral parts of the retina are subdivided into a germinative zone (gz) and the iris (i).

FIG. 12. The cornea is free from pigment. The central part of the retina is fully differentiated. In the pigment epithelial cell processes corresponding to the visual elements have appeared.

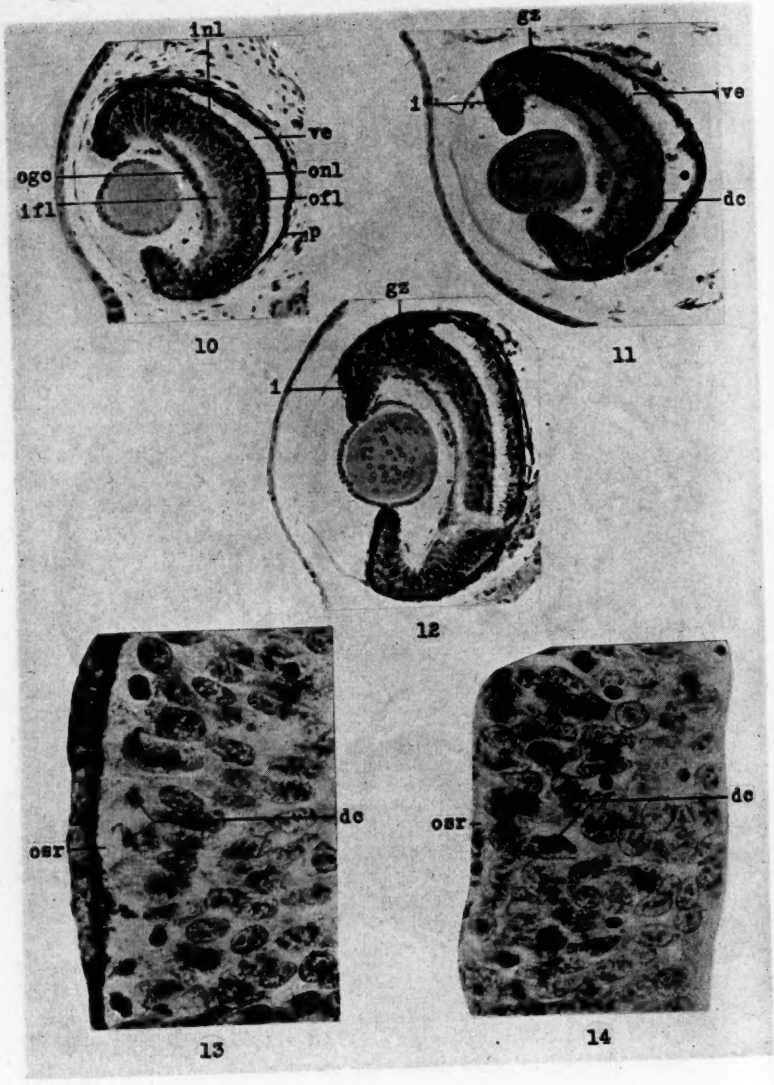
FIG. 13. *Cf.* Fig. 6. Note the pycnotic dividing cells (dc) on the outer surface of the retina (osr).

FIG. 14. *Cf.* Fig. 9. Note the degenerate nuclei (dc) in the future inner nuclear layer.

* For reproduction the plates were reduced to x 0·55 of the original size.

PLATE I

PLATE II



VASONEUROSIS WITH EYE-SYMPTOMS

BY

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PROFESSOR: DR. CONRAD ALBRICH

THE significance of the innervation troubles of the bloodvessels—particularly since Richter's experiments showed that they may be limited to certain regions, even to one of the nourishing-branches—deserves greater attention in the diagnosis of eye disease.

In the following we record a case, which is a most instructive instance of a temporary innervation trouble.

A man, aged 32 years, was several times under our observation, suffering with slight conjunctivitis. He said, he was afraid to open his eyes in the morning, for often he felt pains in them, and they became injected. These symptoms passed away in about one and a half hours. As, objectively, we were never able to see anything more than a slight conjunctivitis, he received suitable treatment. Once, he came to the clinic in the morning alarmed, reporting that he was roused from sleep by the ring of the telephone; when getting up the sunshine suddenly got into his eyes, and consequently he felt the above mentioned symptoms, only much stronger. His right eye got very red, he felt a sharp pain in it, so that he didn't dare to open it, and subsequently felt a violent throbbing in his head.

On examining him we found that the right eye-lids were somewhat swollen, photophobia was present, the conjunctiva injected, and strong ciliary injection. On touching the eyeball the patient complained of great pain. As he was very neurasthenic, we met with great difficulty in examining him at all.

The corneal epithelium was intact. No staining with fluorescein could be seen. The reflex of the cornea was present. Deep in the lower part of the cornea a slight haze was present. Descemet's wrinkles were not noticeable, only a few unusually thick nerves. A regular contour of the endothelium could not be observed. The iris was slightly hyperaemic, no precipitates were present.

Pain in the ciliary region suggested early iritis. The size of the bloodvessels of the eyeground was normal. The tension was 15 mm. Hg in the right eye, and 21 mm. Hg in the left, which was intact. During the attack the blood pressure was 120/80 Hg. A scotoma was not found. Visual acuity was 6/9, and normal in the left eye. Marked fulness and throbbing of the blood

vessels on the right temple was apparent. We kept the invalid in a dark room and observed him every 5-10 minutes. The symptoms vanished before our very eyes. The ciliary injection nearly entirely passed away and the sensitiveness ceased. The throbbing and fulness of the bloodvessels of the temple, which were noticeable some minutes before, ceased, but he felt numbed. Next day the invalid was well, his eyes were normal, his visual acuity became perfect. The tension of the right eye became as normal as the left one (20-21 Hg). The substance of the cornea, as could be seen with the slit-lamp, was clear, the formerly swollen nerves were scarcely visible.

Questioned, the patient stated that these symptoms occurred often but in much slighter degree. His mother and grandfather suffered from migraine. He was a victim of migraine too.

During these above mentioned attacks his head did not ache, he only felt a kind of congestion. He was neurasthenic and showed a vivid dermographismus. Complement fixation was negative.

We knew several members of his family, some of whom were neuropathic, and showed degenerative stigmata.

To explain the symptoms described here, we were facing a case of a transient half-sided bloodvessel crisis, which was caused, as it seems, by certain constitutional changes, connected with reflex causes, which apparently occurred repeatedly. Among the symptoms, that of the transient thickening of the nerves in the cornea deserves our attention, as well as the intermittent œdema of the cornea. The common characteristics of these cases are (13 such cases are mentioned in the literature), that they appear suddenly in the morning, pass away quickly, are connected with œdema of the cornea, with changes of the epithelium and endothelium, and with enlargement of the nerves of the cornea.

But the intermittent œdema of the cornea is never accompanied by signs of irritation or by diminution of the tension. (Aubineau, François, Hambresin.) The above-mentioned case is only like the transient œdema of the cornea, it occurs in the morning, and is characterized by a temporary phase. However, these cases differ on the grounds that diminution of the tension, and strong injection, are signs of an acute circulatory trouble. These symptoms remind us rather of the intermittent form of ophthalmomalacia. Reis, according to his observations, states that ophthalmomalacia can appear in various forms. According to him the entire groups of corneal changes which are of the same nature, and are mentioned in the literature under various names, such as "Buchstabenkeratitis" described by Haab, the "Gitterförmige Hornhauttrübung" by Caspar, the neuritis cornealis and so on, as well as ophthalmomalacia, are due to neurotic causes.

Undoubtedly the essence of the case described here, was vaso-neurosis, involving lessening of the bloodvessel-tone. Whether we consider this syndrome as ophthalmomalacia, or intermittent corneal œdema, it is essential to mention the researches, which reveal the above mentioned clinical symptoms. In these researches the authors naturally were examining the part played by the endothelium of the cornea. Fuchs stated that in the human eye, the aqueous could not enter the cornea after destruction of the endothelium; but against this, are the researches of Hippel, Bullot, Lohr and Graf and the statements of Fischer, which show that a diminution of concentration of the aqueous humour amounting to 0·05 per cent. causes œdema of the cornea. The authors think that the primary change is imbibition of fluid by the cornea as a result of changes in the innervation of the blood-vessels. The concentration of the aqueous is thus reduced, with resultant changes in the endothelium.

In consequence of the endothelial-barrier trouble, the substance of the cornea becomes imbibed, the "Leitplasmodium" (Nageotte, Reiser) which envelops the nerves will also be œdematous. That is why the corneal nerves swell during the blood vessel crisis and they are well visible aided by a slit-lamp. However, this disappears when the fit passes.

Though the symptoms of our case remind us of intermittent corneal œdema, yet we think it more suitable to consider it as a variety of ophthalmomalacia, because an obvious formation of Descemet's wrinkles could not be seen during the observation of the patient. Perhaps, we might take the mixed symptoms of both diseases of the cornea as an intermittent form of corneal œdema, differing only in quantitative degree from the well-known troubles of ophthalmomalacia, described by older authors.

It would be rather difficult to dispute the independent thoroughness of the two diagnoses. Their mutual feature is, that both are originated by neurological causes. That notion in connection with the case of our patient we can verify.

Taking the blood vessel troubles into consideration, which occur in the family of the patient, the case is due to an inherited constitution, as the cause of the vegetative stigmatisation.

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LENS SLIDING IN REMOVAL OF CATARACTS

BY

E. W. ARNDT

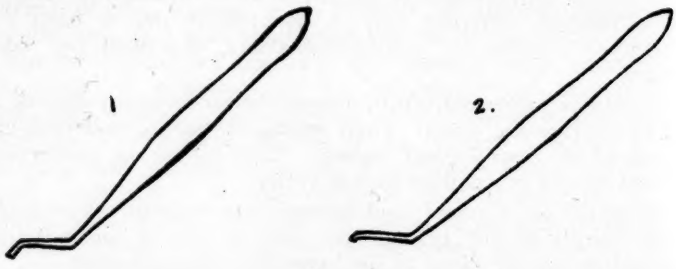
COLOMBO*

IN this article, I wish to give my experiences of a little modification in the operation for removal of cataracts in capsule, where the lens is slid out over the iris, with the hope that it may be of use to other operators. So many methods have been described in the past that one hesitates to add further to the subject, were it not that the usefulness and simplicity of this method appear to warrant its description, complications are negligible, and the instruments required are just those in every day use, with the addition of the special, simple, forceps, about to be described.

I have found this method particularly useful for removing cataracts that are not advanced, but yet handicap the patient considerably.

Early in 1936 a modified Hess forceps was used by me, which gave a fair measure of success. This was made by Messrs. Carl Reiner of Wien, who did an excellent bit of work. The alteration consisted in shortening the terminal part of the forceps so as to allow of its being easily introduced into, and removed from, the anterior chamber, without touching the iris or unduly pressing the cornea back.

The accompanying sketches show the alteration.



The sharp teeth were on purpose made blunt by me as they used to cut through the capsule while it was being drawn upon. Owing to this draw-back, I had a similar forceps made, with the difference that the sharp points were replaced by two oval surfaces similar to those of Arruga's forceps—this was done for me by

* Now of Claremont, Perth, West Australia.

Messrs. Down Bros., these forceps have been in constant use since they reached me in November, 1937, and have given great satisfaction.

TABLE I

Since November 1, 1937, to October 31, 1938.

A.

Total number of cataract cases operated on (excluding congenital) 254
of these

	Per cent.
a. extraction in capsule without iridectomy	81=31·88
b. extraction in capsule with peripheral iridectomy	54=21·25
c. extraction in capsule with total iridectomy	4= 1·57
d. extraction in capsule with or without iridectomy, capsule burst, and was removed entire at the time	29=11·40
	168
e. extraction with or without iridectomy and with capsulotomy	86=33·90
	254

complications which occurred in these operations are shown in the following table—the letters corresponding to the type of operation mentioned in Table I.

TABLE II

	Iris stroked down	Excision prolapsed iris	Peripheral iridectomy	Needling of capsule	Vitreous escape	"Vitreotomy"	Retinal detachment
a.	7	–	4	–	2	2	–
b.	2	3	–	–	1	1	1
c.	–	–	–	–	–	–	1
d.	1	–	–	–	1	1	–
e.	1	–	1	4	2	2	1

B.

Total number of cataract cases operated on between June, 1936,–November 1, 1937 359

of these, extraction in capsule were 115

A short note of explanation regarding these cases of extraction: every case is approached with the idea of removing the cataract in capsule, and efforts to this end are made but not persisted in,

if any danger to the eye is seen to arise in the course of the operation. Hence, the type of operation finally done depends on the behaviour of the eye during the operation.

The forceps already described is used, and a conjunctival bridge is formed in every case.

It happens in certain cases that the capsule tears off in the grip of the forceps, the case then becomes a straight forward one of extraction with capsulotomy, the fairly large bit of capsule that is torn off allows easy delivery of the lens.

At times the capsule bursts while the lens is passing through the corneal section and comes away entire in the forceps, or can be removed entire with suitable forceps after the lens matter is cleared (*d* in Table I), if there is a hard nucleus it continues to slide out over the iris, if soft matter alone, it is pressed out or washed out of the anterior chamber. I have included *d* in Table I under the head " removal in capsule."

In the *Trans. Ophthal. Soc. U.K.*, 1936, pp. 337-338, H. Horsman McNabb mentions his operation of extraction in capsule without tumbling the lens, and states that Professor de Grosz of Budapest operates in a similar way.

In this operation done by me since 1936, the lens is not tumbled but is slid out over the iris, an easy, straight-forward method, which causes no damage to any part of the eye and leaves the vitreous face absolutely flat and unaltered. I realise, however, that this is not an operation for beginners, previous experience of cataract operations and a very light touch being essential.

Preparation

The day before the operation after the usual attention to lids and lashes, the pupil is fully dilated with a 1 per cent. atropine solution used morning and evening. Early in the morning of the operation atropine is again instilled once.

At the operation, the eye is anaesthetised with cocaine drops 4 per cent. and adrenalin, and eserine drops ½ per cent. instilled just before the section is made.

The facial nerve is blocked by van Lint's method of injection in the temporal region, which we find ample for all purposes.

The Operation

The eye being ready for operation, a speculum (Smith's-spring) is introduced, and after the corneal section is made at the limbus, is held off the eye by an assistant. A conjunctival bridge is always formed as it is an excellent means of keeping the corneal flap in position, and acts favourably in other ways.

Next, the conjunctival bridge is gently lifted off the eye with a

Bowman's spoon, the special forceps introduced with closed blades into the anterior chamber till the ends touch the capsule, the blades are then opened and the capsule is seized at its middle, in a firm yet light hold.

The lens is now drawn gently and evenly to one side in the horizontal meridian, say " 3 o'clock," till the zonular ligament gives at the opposite point, *i.e.*, " 9 o'clock " the movement is next in the opposite direction, slow, even, continuous, and again the ligament gives, this time at " 3 o'clock." Now the lens is drawn upwards, *i.e.*, towards " 12 o'clock " and the ligament ruptures at " 6 o'clock," the edge of the lens often presenting, lastly, the lens is gently pushed in the opposite direction, *i.e.*, towards " 6 o'clock " and the last part of the ligament gives at the upper pole, and the edge of the lens presents again, tending to ride over the iris. As this happens, gentle pressure is made on the sclera under the conjunctival bridge, with Bowman's spoon, which up to this point has been lifting the conjunctival bridge up, and the lens is gently slid over the iris by a very light pulling movement directed through the forceps, and easily delivered, any remaining few fibres of the zonular ligament giving way at this stage. When the lens is out the iris will be found to lie back flat on the vitreous surface, and the pupil is quite regular in outline. In a few cases it is necessary to stroke the upper part of the iris gently into position, or in some cases where the iris is judged to be slack, a peripheral iridectomy is done.

With this, the operation is complete, a few drops of eserine ½ per cent. are again instilled, a little boric ointment smeared over the wound, and the eye is closed.

Total iridectomy is very seldom performed and only in such cases where the pupil does not dilate in spite of several instillations of atropine, or where some complication exists, or perhaps accidentally in a difficult patient.

The main point in this operation is the necessity for deliberate, even, gentle and continuous movements from the time the capsule is held till the lens is out. If the capsule ruptures during the operation, it either comes away entire in the forceps, and the lens matter is easily evacuated, or, the operation becomes a straightforward extraction with capsulotomy.

The following morning when the eye is dressed, it is found to show very little post-operative reaction, the anterior chamber is well formed, and the pupil is round and small. Given a docile patient, with ordinary care, he is ready to leave hospital in about 10 days, sight at this time being anything from 6/36 to 6/6. With time, sight improves. A few cases do show what may be termed complications, which, however, are not peculiar to this type of operation, and are remediable.

TABLE III

1. Slight haemorrhage into the anterior chamber.
2. Vitreous escape.
3. Shallow anterior chamber.
4. "Sublapse" of iris, and very rarely a prolapse of iris.
5. Glaucoma.

1. *Blood in the Anterior Chamber.*—A rare condition and often due to a little blood finding its way in at the time of the operation, from the section. It gets absorbed easily. Wright of Madras in describing his operations on South Indians, where he used a conjunctival bridge, attributed it, if I remember rightly, to some peculiarity in the blood or the condition of the blood vessels. We have not had this experience in our South Indian patients, of whom we get a good few.

On the other hand, in cases of general disease, *e.g.*, diabetes or kidney trouble, blood in the anterior chamber is more serious, specially in the latter condition. Here, we find calcium of assistance, in addition to continuation of treatment of the general condition.

2. *Vitreous Escape*—is again a very rare complication.

4 out of 168 cases in intracapsular operation
or 6 out of 254 cases in all.

The escape of vitreous may vary in size from that of a small bead to a pea. If the lens has been delivered, the eye is closed at once for a few minutes, then very gently opened and examined. If the lips of the corneal wound are found to be in apposition, the eye is again closed and the usual dressing applied. If the lips are not in apposition, any protruding vitreous is cut away with scissors, the parts stroked into position and the eye closed.

In Table I, three cases of vitreous escape consisted of tiny beads which settled back into the eye and allowed the corneal wound to heal without further disturbance.

However, it was found later that the pupil was drawn up slightly and pear shaped, owing to a very fine attachment of the vitreous to the corneal wound at the spot at which it presented during the operation. No operator feels comfortable at the thought of vitreous caught up in the wound, no matter how slight, and there is the cosmetic appearance to consider as well.

In such cases, a minor operative procedure is carried out. We pass a blunt Lang's knife into the anterior chamber and sever the vitreous thread at its attachment to the corneal wound. This successfully does away with any after danger and leaves a round normal pupil. We call this vitreotomy—rather a cumbersome name.

3. *Shallow Anterior Chamber.*—A few cases occur from time to time, if the iris and vitreous are clear of the corneal wound,

the condition is of no consequence and settles down in a few days. The patient is best kept in bed during this time. I have detected no cause for this shallowness, there is no detachment of retina or choroid, and the whole eye looks normal but for the shallow anterior chamber. The tension is slightly below normal in such cases, till the chamber reforms.

On the other hand, a shallow anterior chamber due to a small detachment of the choroid or retina in the periphery is more serious, two cases out of 168 intracapsular operations or three cases in 254 operations in all.

Fortunately, this is a rare occurrence and those I have met with have all settled down normally and had no further trouble, even years after. The treatment consists of complete rest in bed, use of Lochbrille spectacles in more pronounced cases, and, we use calcium intra-muscularly. We feel that calcium has been of assistance, and continue to use it. Omnadin and such like preparations appear to be definitely contraindicated, as they seem to increase the detachment. Any operative procedure for this condition is not to be thought of, no matter how tempted one may be to try it, as a lasting, completely satisfactory result, is obtained with rest and patience. My last case had four large balloon detachments from " 2 to 5, and 7 to 11 o'clock." These came on a fortnight after the operation, which was a perfectly straight-forward one. The patient was old, emaciated and very weak. I managed to induce him to lie up for three months and at the end of that time there was perfect reposition and vision was 6/6 and J.1. This was an exceptional case, the usual period of rest is about a month.

Here again I wish to stress the point that this condition is not peculiar to this type of operation, as I have met it in cases operated on with capsulotomy.

4. *" Sublapse " of iris and rarely prolapse of iris.*—Regarding what we call a " sublapse " of the iris in contra-distinction to a prolapse—In this condition the periphery of the iris is found to be displaced forwards lying up against the cornea at the limbus, the pupillary part lies free, and the pupil is slightly oval in shape (10 out of 168 operations).

A definite prolapse under the conjunctival bridge, or to one or other side is rare (3 out of 168 intracapsular operations) and has to be excised.

The treatment carried out in cases of " sublapse " is to pass a blunt Lang's knife into the anterior chamber at a little distance from the " sublapse " and stroke the iris down towards the pupil. The adhesion between iris and cornea gives easily and a flat iris with round pupil results. Eserine is required for a few days and the patient should be kept quiet. This little procedure is done at

the end of a week after the major operation, I have, however, done it a month after the extraction, and found little difficulty in accomplishing it. Seldom is an iridectomy required (4 cases in 168) and there is no difficulty in doing one, if it is judged necessary. This little procedure is termed " stroking down of iris " and is shown in Table II column 1.

5. *Glaucoma.*—A. Secondary to some cases of:—

(*a*) definite prolapse of the iris.
(*b*) a fairly large sublapse left uncorrected.
(*c*) prolapse of vitreous.

B. Primary—with no evidence to account for its occurrence. Both kinds of glaucoma have been met with, and here again, are not peculiar to this type of operation.

Under Class A the treatment is obvious and has already been discussed. As regards the very few cases of primary glaucoma for which no cause can be detected, corneo-scleral trephining or cyclodialysis cures the condition.

In the last case of this nature, a recent one, the anterior chamber appeared quite normal, the iris flat, pupil round and reacting normally, the fundus showed few haemorrhages and few points of exudate. The patient was diabetic, the percentage of urinary sugar varying from 0·5 per cent. to 3 per cent.

After treatment for some time with miotics and dextroglaucosan, cyclodialysis was performed, as it was considered unsafe to venture on a bigger operation. The result is satisfactory so far, the tension of the eye varying now from 15 to 18 (Bailliart). After the operation, the haemorrhages and exudates increased considerably, reducing vision from 6/12 to 6/60.

The success of this method of sliding cataracts over the iris, with a special forceps, depends on

(*a*) the condition of the lens capsule.
(*b*) the condition of the zonular ligament.

The former can be gauged more or less with a little experience. The hypermature cataract with changes reaching up to the capsule, the fluffy type where the lens is quite white and the matter has a flocculent appearance, are not always successful, as the capsule ruptures easily. In Morgagnian cataracts, the chances are equally divided. Immature cataracts give the greater number of successes. Here, however, the condition of the zonular ligament is of importance, as it is found that in early cases of immature cataract the ligament is usually tough. Conditions in such cases vary a good deal, hence the necessity of not expecting every attempt at delivering a lens in capsule to succeed, but of adapting the type of operation to the response of the eye during the operation.

ANNOTATION

The Journal in 1940

When the War came last year it was obvious that some curtailment in the size of the monthly numbers would have to be made, since the management could not foretell the financial position with any exactitude.

It is now possible to state that we shall be able to continue regular publication at any rate for this year, and every effort will be made to continue for the "duration." But the rationing system must continue, although it will be our aim to make this ration as large as possible. Papers dealing with war conditions will have priority over more ordinary material.

In these circumstances some delay in publishing papers is inevitable. We hope authors will bear this in mind and the Editors on their side will do their best to avoid undue delay.

Authors can help the Journal materially by keeping their proof corrections as low as possible. Manifest errors must of course be corrected, but there is no need to make endless corrections in the interests of the English language. The Editors feel that they can almost pardon a split infinitive in the cause of economy. And the writer has always had a sneaking sort of partiality for that old Kaiser Sigismund, who at the Council of Constance in 1414, was pulled up by one of the Cardinals on an obvious slip in grammar and replied "I am King of the Romans and *super grammaticam*." It is so easy to make mistakes not only in professional matters but also in writing and speaking.

ABSTRACTS

MISCELLANEOUS

(1) **Cecchetto (Verona).—Paracentesis of the anterior chamber in the treatment of various ocular diseases. (La paracentesi della camera anteriore nelle piu svariate malattie oculari).** *Rass. Ital. d'Ottal.*, January-February, 1939.

(1) The value of this remedy, which goes back to Galen, is insufficiently recognised, says **Cecchetto**; it is of great use in many ocular conditions. The changes in the eye after paracentesis have been studied by several authors, both those after a single operation and those which follow repeated paracentesis. There is little doubt that the aqueous is formed by the ciliary body; Greeff

noted that after the anterior chamber is emptied, bullae form all over the ciliary region; the epithelium of the ciliary processes is raised into bullae visible to small magnification, and containing masses of coagulated material. The bullae burst and the contents are thrown into the aqueous. This is seen within a few minutes of the paracentesis. Other observers have repeated the paracentesis daily for a number of months, and find that the ciliary body is more developed than that of the control eye. The iris also, is thickened to three times its normal; this seems due to an increase of the connective tissue; there was an increase in the number of vessels of the iris; from these changes it may be gathered that repeated paracentesis increases the activity of the metabolism of the iris and ciliary body and causes hypertrophy of the stroma and the vessel walls. It is easy to see how the eye may benefit from the increased activity.

The author uses paracentesis not only in chronic and infantile glaucoma—in which conditions he claims great gain from its employment—but also in many conditions where the uveal tract seems to be working insufficiently. In a number of cases of high myopia with macular change and vitreous floaters, he has found it helpful. In most of these cases other remedies also were applied and therefore it remains in doubt how much is to be ascribed to the operations. The author has had good results in retinitis pigmentosa and promises to give these in a later paper.

HAROLD GRIMSDALE.

(2) **Borsotti (Geneva).—The importance of over-action of the inferior oblique in the surgical treatment of paralysis of the superior oblique. (L'importaza del riconoscimento della iperfunzione del piccolo obliquo nel trattamento chirurgico delle paralisi del grande obliquo).** *Rass. Ital. d'Ottal.*, March-April, 1939.

(2) This paper is a corollary to that recently appearing in the *Ann. d'Ottal.* In it **Borsotti** re-states the difficulties in diagnosis of loss of power of a vertical motor muscle; he points out that the probability of injury to the superior oblique is much greater than that of injury to a single rectus muscle, since the former is supplied by a nerve which has no other muscle to supply, while the recti are a group supplied by one nerve. He passes shortly over the methods which have been proposed for the relief of the symptoms and decides that no operation is so successful in removing them as weakening the inferior oblique when there is manifest over-action of this muscle. He shows how careful examination of the diplopia and especially of the cyclophoria will show this over-action, and gives account of cases in which myectomy of the inferior oblique gave relief. The operation is conducted as follows: after subcutaneous injection of the anaesthetic, an incision is made along the

inner half of the inferior orbital border. The middle of this incision should be a line dropped vertically from the supraorbital notch. The skin and subjacent orbicularis are separated down to the periosteum, then by means of squint hook the tendon and muscle of the oblique is picked up; a portion some 7 to 10 mm. wide is excised from the belly of the muscle.

In the cases in which over-action of the inferior oblique was definite, the operation was followed by great relief; in most cases the troublesome cyclophoria is corrected; it is true that recession of the inferior rectus of the opposite side would seem theoretically to be the best method of correction, but this takes no account of the over-action of the inferior oblique, which almost constantly accompanies paresis of the superior. In this paper, as in the former, he gives as an appendix, Franceschetti's chart for the diagnosis of paresis and over-action of the various vertically moving muscles.

HAROLD GRIMSDALE.

(3) **Agnello (Addis Ababa).—Toxic amblyopia from filix mas. (Amaurosi tossica da felce maschio).** *Rass. Ital. d'Ottal.*, March-April, 1939.

(3) The use of filix mas as a vermifuge is attended with risk of toxic amblyopia especially if the drug be allowed to remain for any length of time in the bowels; in the case recorded by **Agnello** the patient had passed a large worm, and was then given a large dose of filix mas; in a few hours he became comatose and on recovering consciousness, found himself quite blind. Ophthalmoscopic examination showed slight retinal oedema; the arteries were a little reduced in size, the macula standing out as a cherry red spot. There was no recovery of sight. The discs became atrophic. The author discusses the action of filix mas, contrasting it with that of quinine; he thinks that the blindness cannot be due to anaemia from constriction of the arteries but that the drug must have an elective action on the fibres of the optic nerve. The author points to the necessity of removing the drug from the bowels soon after ingestion by appropriate purgatives.

HAROLD GRIMSDALE.

(4) **Contino (Palermo):—The visibility of the hyaloid canal. (La questione della visibilita del canale ialoideo).** *Ann. di Ottal.*, January, 1939.

(4) **Contino** gives an account of all the forms which the hyaloid canal may take, and discusses their origin. He gives an account of two cases which have come under his observation; he shows how the canal may become visible as the result of vitreous haemorrhage and may be lost again when the blood is absorbed.

HAROLD GRIMSDALE.

(5) **Tita (Catania).—Primary glioma (spongioblastoma) of the optic nerve with "meningiomatosis" of the sheaths. (Glioma, spongioblastoma mono-polare astrocitario, primitivo del nervo ottico, con "meningiomatosi" della guaine).** *Boll. d'Ocul.*, April, 1939.

(5) The patient to whom this report refers, was a small boy brought by his mother who had noted that his divergent and prominent left eye had lost all sight. There was nothing to be felt in the orbit. Movement of the eye was possible in all directions but was limited in all. There was complete atrophy of the papilla. There was no sign of involvement of any accessory sinus. The growth seemed to be in the orbit only; by Calderaro's method the soft parts making the anterior wall of the orbit, including the eye, were turned to one side and the contents of the orbit removed. The cavity was almost filled by a mass, the coats of which were ruptured by the finger in isolating it. It was clear that the optic nerve was the source of the mass; no trace of the nerve could be found except for a few millimetres where it was attached to the eye. The wound healed well; there was a trophic keratitis after the operation, but this cleared. Examination of the growth showed that it was primary spongioblastoma of the nerve. The nature of the changes in the sheath of the nerve is not easy to explain. After considerable discussion, **Tita** leaves the matter still unsolved. The paper is well illustrated with micro-photographs of the tumour.

HAROLD GRIMSDALE.

(6) **Haster, W. T. (Everett, Washington).—Standardization of the preparation of eye-drops.** *Amer. Jl. Ophthal.*, Vol. XXII, p. 423, 1939.

(6) **Haster** comments on the contamination of preparations of eye-drops used in hospital and private practice. It seems that after the drops have been used once or twice bacterial cultures are positive, and later molds and fungi may occur, particularly is this so in damp climates.

He recommends the use of a Nipagin-Nipasol combination as a germicide and preservative. These substances are the ester derivatives of benzoic acid, Nipagin-m is p-oxybenzoic acid-methyl ester and Nipasol-m is p-oxybenzoic acid-propyl ester. The combination is non-poisonous and non-toxic to man, it is harmless as a pharmaceutical preservative, two to four times less so than phenol. It was found that 0·05 per cent. Nipagin-m with 0·05 per cent. Nipasol-m in solution killed B.coli and staphylococcus pyocyaneus in six days, and destroyed common moulds, yeasts, fungi and Gram-positive and Gram-negative bacilli.

The author states that Eschenbrenner found it possible to kill resistant spores with a 0·1 per cent. Nipagin-Nipasol solution in 15

minutes by boiling at 100°C. while without using this ester-combination it took four hours to effect the same result.

The author recommends the following dilution for the sterilization of eye solutions:—65 parts Nipagin-m plus 35 parts Nipasol-m. This solution is non-toxic, non-irritating and chemically neutral, it kills staphylococcus aureus in 24 hours and prevents the growth of fungi.

Details are given for the preparation of standard eye-drops, the preparation of an acid buffer solution and an alkaline buffer solution, and there is a table showing the amount of these to be added to the various drugs used in ophthalmic practice.

H. B. STALLARD.

(7) **Greene, L. S. and Perry, N. W. (Washington).—Erythema nodosum with nodules in the conjunctivae.** *Amer. Jl. Ophthal.*, Vol. XXII, p. 389, 1939.

(7) **Greene and Perry** describe the case of a woman, aged 54 years, who developed areas of hyperaemia and nodules in the bulbar conjunctiva of each eye over the insertions of the four recti muscles. These ocular changes appeared simultaneously with the characteristic cutaneous lesions of erythema nodosum affecting the extensor aspects of the forearms and legs, and also with the onset of malaise raised temperature and arthralgia.

The conjunctival lesions were triangular in shape with the base towards the limbus and were localized to the bulbar conjunctiva. They were raised, deep cherry-red in colour, painless and movable over the unaffected sclera. In the centre of the nodules were two to four nodules about the size of a pin's head. A slit-lamp examination of these lesions showed them to consist of a superficial wide meshwork of dark red vessels, a network of small vessels surrounded each nodule, the nodule itself laying in sanguineous fluid. Some of the nodules stained slightly with fluorescein.

Complete recovery occurred eight weeks from the onset of the illness. Treatment consisted of sodium salicylate grs. 45 daily, rest in bed, and hot gargles for the pharyngitis.

The few cases reported in the literature are briefly reviewed.

H. B. STALLARD.

(8) **Persichetti (Rome).—The haemoclasic reaction in luetics with ocular signs. (La reazione emoclasica nei luetici con manifestazioni oculari).** *Boll. d'Ocul.*, March, 1939.

(8) It is well known that when proteins of various kinds, or vaccines are introduced to healthy subjects, there follows almost constantly, a leucocytosis; on the other hand if a subject of certain diseases be injected with the appropriate vaccine or with the

curative drug, there follows immediately a fall in the number of leucocytes; this fall takes place at once and is at height about half to three quarters of an hour after the injection. There follows in a short time a rise to the preceding state.

Persichetti has examined the reaction in a number of cases in which there was a certain history of syphilis; in these, 21 out of 30 were positive showing a reduction of the number of leucocytes by at least 800. Of the cases which did not show the reaction, some were under treatment; this would very probably interfere with the change in the leucocyte count.

Two other series were examined; one showing a negative Wassermann reaction, was considered to be syphilitic; the other was not infected. Of the first who numbered 25, eight were positive; of the normal, none. Comparing the reaction with the Wassermann, it seems clear that in some cases in which the W. R. is negative, this reaction is positive, but it does not seem to be superior to the W. R. in all cases; it would seem at least to be a useful adjuvant where there is doubt.

HAROLD GRIMSDALE.

(9) **Borsotti, (Pavia).—A case of paralysis of the third nerve, with disturbance of swallowing and speaking. (Considerazioni su un caso di paralisi parcellare del III paio con disturbi della deglutizi ne e fonazione).** *Riv. Oto. Neuro. Oftal.*, January, 1939.

(9) The difficulty in the exact diagnosis of nervous lesions is well known. **Borsotti** publishes a case which presented considerable doubt. The man, aged 44 years, had noticed for six weeks a little disturbance in vision which disappeared on closing one or other eye. Recently he had noticed deviation of the left eye outwards with constant double vision, and some drooping of the lid; at the same time he had difficulty in swallowing and his voice had become nasal. He denied lues, and the examination of the blood and cerebrospinal fluid was negative. He was a heavy drinker. The right eye was normal throughout; the left showed paralysis of the internal rectis, and levator palpebrae with paresis of the rectus superior. Further examination showed paresis of the soft plate and of the constrictors of the pharynx; also loss of power over the vocal cords. Treatment by bismuth injections (salbiol) was soon followed by improvement, and this was increased by the additional injection of iodide intravenously. The diagnosis at first was disseminated sclerosis; the rapid improvement was not unlike the course of this disease; later a possible luetic cerebral lesion, or a toxic neuritis were considered as more probable; it must be remembered that the man was a heavy drinker.

HAROLD GRIMSDALE.

(10) **Nicolato (Pavia).—Some results of reconstruction of the lids after gross losses. (Considerazione su alcuni risultati di ricostruzione delle palpebre a seguito di gravi traumi).** *Ann. di Ottal.*, February, 1939.

(10) It is not infrequent for patients to suffer a grave deformity of the lids to remain uncorrected, because they fear an operation or some other reason. **Nicolato** holds that it is the surgeon's duty to urge some operation, not only because the condition may lead to damage to the eye, but also because the unsightly appearance is distressful to the friends.

The choice of operation is not always easy and no one method is applicable to all defects. The author prefers, where possible, to use Dieffenbach's or Fricke's method, so as to obtain the skin to form the new lid from some near region; but on occasion he uses Gillies's plan of tubular grafts taken from a distance. He lays stress on the necessity of making the flaps large enough, cutting them with curved outlines to preserve as far as possible their blood supply if the base must be twisted. He advises that all bleeding be carefully stopped by pressure or torsion of the vessels; ligatures must be avoided. Sutures must be put in carefully; those needed to fix the flap in position should be stronger than those which bring the edges together. Tarsorrhaphy is needed in most cases and should remain undivided for two months.

A number of photographs are given showing the excellent results obtained, and in some cases the various stages of the procedure.

HAROLD GRIMSDALE.

(11) **Schumacher, G. (Basle).—Monocular and binocular threshold values in dark adaptation of the eye in day vision and night vision. (Ueber des Verhalten der monokularen und binokularen Reizschwelle während der Dunkeladaptation des Tagesund Dammerungsapparates).** *Acta Ophthal.*, Vol. XV, p. 1, 1939.

(11) **Schumacher** reviews the literature on the subject of binocular summation on which discordant results are reported except that there is agreement that in foveal day vision there is no binocular summation. On an exhaustive re-examination of the whole subject he concludes that (1) the apparatus for scotopic vision shows binocular summation. (2) There is no such effect in the photopic apparatus. (3) Summation in the scotopic eye is less marked at the beginning of dark adaption than after 45 minutes, when the monocular threshold value is practically double that of the two eyes together. (4) There is an inter-relationship between the scotopic and the photopic apparatus, influencing the reactions of the photopic apparatus.

ARNOLD SORSBY.

(12) **Möller, H. U. (Copenhagen).—Symptoms simulating glaucoma in a case of chordoma. (Symptômes, simulant de glaucome, dans un chordome du clivus blumenbachii).** *Acta Ophthal.*, Vol. XVII, p. 20, 1939.

(12) **Möller** recalls the work done on pseudo-glaucomatous cupping and emphasises Traquair's view that an arcuate scotoma by itself is not pathognomonic of glaucoma. He describes in detail the clinical and histological findings in a case showing cupping and optic atrophy suggestive of glaucoma, arcuate scotoma, but no increase of intra-ocular tension. The condition was ultimately established as due to a pituitary lesion.

ARNOLD SORSBY.

(13) **Karbowski, M. (Warsaw).—Iontophoresis in ophthalmology.** *Ophthalmologica*, Vol. XCVII, p. 166, 1939.

(13) In a detailed discussion on the methods and scope of iontophoresis, **Karbowski** emphasises the greater therapeutic effect of ionised substances, especially the ions of calcium, potassium, adrenaline, atropine and pilocarpine. He stresses in particular the value of adrenaline ionisation which surpasses the effect of subconjunctival injection.

ARNOLD SORSBY.

(14) **Igersheimer, J. (Istanbul).—Can glaucoma influence transudation from retinal vessels? (Ist ein Glaukom imstande, die Transudation aus den Netzhautgefässen zu beeinflussen?).** *Ophthalmologica*, Vol. XCVII, p. 146, 1939.

(14) **Igersheimer** gives the clinical and post-mortem findings in a patient, aged 42 years, who had shown severe vascular hypertension with uraemia. During the last eighteen months of life glaucomatous excavation was present, but there was no retinal change. He discusses the question of whether the absence of transudates is to be explained by the co-incident presence of the glaucoma.

ARNOLD SORSBY.

(15) **Redslob, M. E. (Strasbourg).—The teeth and optic nerve. (Les dents et le nerf optique).** *Ophthalmologica*, Vol. XCVII, p. 133, 1939.

(15) **Redslob** reports a case of retrobulbar neuritis in which both nerves were attacked within an interval of two years. On each occasion recovery took place after extraction of an infected tooth, improvement setting in within a few hours and full vision being restored within four or five days. He accepts this as conclusive proof of causality and discusses the possible mechanism. He inclines to the probability of angiospasm in the retrobulbar part of the nerve set up by reflex irritation, or alternatively to a local allergic reaction.

ARNOLD SORSBY.

BOOK NOTICES

Transactions of the Ophthalmological Society of the United Kingdom. Vol. LIX. Part II. London: J. and A. Churchill. 1939.

The second part of the Transactions for last year forms a bulky volume of more than 500 pages. As is usual it contains the papers read at the Oxford Congress and those of the Midland, Irish and South African Ophthalmological Societies. The bulk of the book is so much increased because of the inclusion therein of the Treacher Collins Prize Essay on "Cerebro-Spinal Disease and its relation to the Optic Nerve," by Dr. T. Hewitson Brown. This accounts for about a third of the whole volume. It is profusely illustrated and contains, besides figures and charts in the text, no fewer than eleven colour plates. It is, we think, the most masterly essay we have ever read and it adds greatly to the value of the Transactions. Another fine paper is the Doyne Memorial Lecture by Williamson-Noble. The discussions at Oxford were on orthoptic training and miners' nystagmus, while the papers by Sir Arnold Lawson and W. H. McMullen, at Oxford, and that of Professor Lindner, at Dublin, are all of a high standard.

The index is a complete one for both parts of the year's transactions, the pagination of Part II being rendered in Clarendon type.

The National Register of Medical Auxiliary Services. Orthoptists. British Medical Association, London. 1940.

A review of the second edition of the National Register of Medical Auxiliary Services appeared in our columns last year, p. 357. In it we expressed the hope that future editions would include the names of those undertaking orthoptic training. The Board of Registration of medical Auxiliaries has lately recognised the British Orthoptic Society as a qualifying body in orthoptics, and members of the Society have been enrolled in the National Register. This Orthoptic Supplement to the Register is the result, and will be most welcome to all ophthalmic surgeons. The number of registered orthoptists is not large and all the more is it essential for surgeons to be able to get the names and addresses of those who are qualified and registered.

Copies of the supplement can be obtained by application to the Registrar, Board of Registration of Medical Auxiliaries, British Medical Association House, Tavistock Square, London, W.C.1.

Bothman's Fundus Atlas. The Year Book Publishers, Inc., Chicago. 1939.

This atlas consists of 50 original stereoscopic photographs. The author is clinical Professor of Ophthalmology in the University of

Chicago and his name is coupled on the title page with that of Reuel W. Bennett, Photographer for the Division of Ophthalmology in Chicago.

Not all diseases found in the fundus are illustrated, but those chosen show all important congenital anomalies and fundus diseases. The photos are in black and white and are printed on photographic paper. Dr. Bothman holds that what is lost by the absence of colour is more than compensated for by accuracy and depth perception. They were taken with the reflex free Nordenson Fundus Camera and were magnified three or more times the size of the original negative with a special stereoscopic enlarger devised by Reuel W. Bennett. The results approximate the fundus picture seen with the red-free light.

The photos are mounted at the bottom of stout cards measuring 9 × 7 ins., the upper part of each card contains details of the history and examination, together with very full description of the condition shown.

The results maintain a high level of excellence throughout; the pictures of glaucoma cupping and congenital posterior staphyloma certainly bear out the author's contention as to depth perception.

In this country we are, of course, more used to fundus atlases in colour, but no one can examine these pictures of Dr. Bothman without recognizing their excellence and faithfulness of detail.

The atlas is procurable in England from H. K. Lewis & Co. and we are kindly informed by them that the English price is £5 10s.

CORRESPONDENCE

To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.

DEAR SIRS,—I shall feel much obliged if you would kindly put in an enquiry in your valuable Journal to know from your numerous readers the following:—In your practice of refraction which of the following conditions you find is more common:

1. Plus cylinder axis 180° or plus cylinder axis 90°.
2. Minus cylinder axis 90° or minus cylinder axis 180°.

In almost all the test-books it is mentioned that plus cylinder axis 90° or minus cylinder axis 180° are more common.

In my practice in Northern India I find that the reverse condition is more common, that is, plus cylinder axis 180° and minus cylinder 90°.

On hearing from you I shall be glad to send you my statistics and my paper on this subject for publication. The paper will be of

interest in case the observations in England are not in conformity with those of mine. In case the observations in England happen to conform we shall have to find reasons for the statements in the text-books.

Yours truly,

RAM KISHAN HANDA.

MASSY GATE, RAWALPINDI.
January 19, 1940.

OBITUARY

R. J. LYTHGOE

The untimely death of R. J. Lythgoe is a tragedy not only to his relations and friends, but also to science. The experimental study of the special senses has been grievously neglected in England both by physiologists and psychologists. Until comparatively recently our knowledge of visual phenomena under different conditions of illumination, etc., was advanced mostly by physicists, generally inspired by practical problems of artificial lighting, and often vitiated by ignorance of the extremely complicated anatomical and physiological facts which determine the neural and psychological responses. Lythgoe took up these problems at the outset of his work as a Beit Research Fellow. That he was able to devote himself unremittingly to them to the end of his life is due to the encouragement he received from the Medical Research Council, and the permanency of tenure of his post under their aegis. His paper on "The adaptation of the eye: its relation to the critical frequency of flicker" in 1929, embodying the results of experiments conducted with the help of his future wife, Miss K. Tansley, revealed new facts in a domain already thoroughly exploited by physicists—facts heartily accepted by them owing to the care and accuracy of his physical measurements. The same accuracy and originality were displayed in his paper on "The measurement of visual acuity," also published in the Special Report Series of the Medical Research Council, in 1932. Both these papers mark new stages in the history of the scientific investigation of visual capacity. During the last few years Lythgoe has been engaged in collaboration with Goodeve and others in an exhaustive investigation of the physical and chemical properties of visual purple and its decomposition products under the influence of light. These researches have been published in the *Proceedings of the Royal Society* and the *Journal of Physiology*. They too reveal a stride forward in our knowledge.

Whilst those who knew him personally mourn the loss of a lovable, modest and retiring searcher after truth, science loses an original thinker and expert craftsman who, had he lived longer, would have stimulated others to follow in his footsteps. More truly than in most cases it may be said that he is irreplaceable.

NOTES

Death

THE death is announced on November 13, 1939, of Professor Anton Elschnig, at the age of 76 years. Most of his professional career was spent in Prague, where he was Professor of Ophthalmology and his reputation in ophthalmology was international. There is an obituary notice of him by one of his old pupils, Karl W. Ascher, in the *American Journal of Ophthalmology*, February, 1940, to which we are indebted for this information.

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Ophthalmological Society of Egypt

THE Annual Congress of the Ophthalmological Society of Egypt took place at the Memorial Ophthalmic Laboratory, Giza, on March 29-30, 1940. The discussion was on blepharitis. The notice reached us too late for insertion in the March number.

FUTURE ARRANGEMENTS

April 25-26, 1940. — Ophthalmological Society of the United Kingdom. Annual Congress.

May 4, 1940.—North of England Ophthalmological Society, at Newcastle-on-Tyne.

July 4-6, 1940.—Ophthalmological Congress, at Oxford.